

## Medical Coverage Policy | Serologic Genetic and Molecular Screening for Colorectal Cancer



**EFFECTIVE DATE:** 01 | 01 | 2022

**POLICY LAST UPDATED:** 08 | 03 | 2022

### OVERVIEW

It is well established that early detection of colorectal cancer (CRC) reduces disease-related mortality. For patients at average risk for CRC, organizations such as the U.S. Preventive Services Task Force have recommended several options for colon cancer screening. Currently accepted screening options for CRC include colonoscopy or sigmoidoscopy, fecal occult blood testing, and fecal immunochemical testing. However, many individuals do not undergo recommended screening with fecal tests or colonoscopy. A simpler screening blood test for genetic alterations associated with non-familial CRC may have the potential to encourage screening and decrease mortality if associated with increased screening compliance. Genetic testing is also being investigated to guide therapy.

### MEDICAL CRITERIA

#### Medicare Advantage Plans

BeScreened™–CRC test may be considered medically necessary when the Medicare Advantage Plans medical necessity criteria is used for review, found in the Medical Necessity policy. Please see Related Policies section.

#### Commercial Products

Not applicable.

### PRIOR AUTHORIZATION

#### Medicare Advantage Plans

Prior authorization is required for the following test(s):

- BeScreened™–CRC test

#### Commercial Products

Not applicable.

### POLICY STATEMENT

#### Medicare Advantage Plans

The following test(s) may be considered medically necessary when the medical criteria in the Medical Necessity policy are met:

- BeScreened™–CRC test

The following test(s) are covered without an authorization requirement:

- SEPT9 methylated DNA testing (eg, ColoVantage®, Epi proColon®)
- Blood-based Biomarker Tests

#### Commercial Products

The following test(s) are not medically necessary as the evidence is insufficient to determine that the technology results in an improvement in the net health outcomes:

- SEPT9 methylated DNA testing (eg, ColoVantage®, Epi proColon®)
- Gene expression profiling (eg, ColonSentry®)
- BeScreened™–CRC test

### COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage, or Subscriber Agreement for applicable not medically necessary/not covered benefits/coverage.

## BACKGROUND

### Colorectal Cancer

For patients at average risk for colorectal cancer (CRC), organizations such as the U.S. Preventive Services Task Force have recommended several options for colon cancer screening. The diagnostic performance characteristics of the currently accepted screening options (ie, colonoscopy, sigmoidoscopy, fecal tests) have been established using colonoscopy as the criterion standard. Modeling studies and clinical trial evidence on some of the screening modalities have allowed some confidence in the effectiveness of several cancer screening modalities. The efficacy of these tests is supported by numerous studies evaluating the diagnostic characteristics of the test for detecting cancer and cancer precursors along with a well-developed body of knowledge on the natural history of the progression of cancer precursors to cancer. Early detection of CRC reduces disease-related mortality, yet many individuals do not undergo recommended screening with fecal occult blood test or colonoscopy. A simpler screening blood test may have the potential to encourage screening and decrease mortality if associated with increased screening compliance.

### SEPT9 Methylated DNA

ColoVantage (various manufacturers) blood tests for serum Septin9 (*SEPT9*) methylated DNA are offered by several laboratories (ARUP Laboratories, Quest Diagnostics, Clinical Genomics). Epi proColon (Epigenomics) received U.S. Food and Drug Administration (FDA) approval in April 2016. Epigenomics has licensed its Septin 9 DNA biomarker technology to Polymedco and LabCorp. ColoVantage and Epi proColon are both polymerase chain reaction (PCR) assays; however, performance characteristics vary across tests, presumably due to differences in methodology (eg, DNA preparation, PCR primers, probes).

### Gene Expression Profiling

ColonSentry (Stage Zero Life Sciences) is a PCR assay that uses a blood sample to detect the expression of 7 genes found to be differentially expressed in CRC patients compared with controls: *ANXA3*, *CLEC4D*, *TNFAIP6*, *LMNB1*, *PRRG4*, *VNN1*, and *IL2RB*. The test is intended to stratify average-risk adults who are non-compliant with colonoscopy and/or fecal occult blood testing. Because of its narrow focus, the test is not expected to alter clinical practice for patients who comply with recommended screening schedules.

BeScreened-CRC (Beacon Biomedical) is a PCR assay that uses a blood sample to detect the expression of 3 protein biomarkers: teratocarcinoma derived growth factor-1 (TDGF-1, Cripto-1); carcinoembryonic antigen, a well-established biomarker associated with CRC; and an extracellular matrix protein involved in early stage tumor stroma changes.

## CODING

The following code(s) are covered for Medicare Advantage Plans and not medically necessary for Commercial Products:

**81327** SEPT9 (Septin9) (eg, colorectal cancer) promoter methylation analysis

**G0327** Colorectal cancer screening; blood-based biomarker

The following CPT code(s) is covered for Medicare Advantage Plans when medical criteria found in the Medical Necessity policy are met and is not medically necessary for Commercial Products.

This code can be used for BeScreened™-CRC test

**0163U** Oncology (colorectal) screening, biochemical enzyme-linked immunosorbent assay (ELISA) of 3 plasma or serum proteins (teratocarcinoma derived growth factor-1 [TDGF-1, Cripto-1], carcinoembryonic antigen [CEA], extracellular matrix protein [ECM]), with demographic data (age, gender, CRC-screening compliance) using a proprietary algorithm and reported as likelihood of CRC or advanced adenomas

## RELATED POLICIES

Colorectal Screening Mandate  
Genetic Testing Services Policy  
Medical Necessity Policy  
Medicare Advantage Plans National and Local Coverage Determinations  
Preventive Services for Commercial Products  
Preventive Services for Medicare Advantage Plans  
Proprietary Laboratory Analyses (PLA)

## **PUBLISHED**

Provider Update, October 2022  
Provider Update, November 2021

## **REFERENCES:**

1. Yip KT, Das PK, Suria D, et al. A case-controlled validation study of a blood-based seven-gene biomarker panel for colorectal cancer in Malaysia. *J Exp Clin Cancer Res*. Sep 16 2010; 29: 128. PMID 20846378
2. Chao S, Ying J, Liew G, et al. Blood RNA biomarker panel detects both left- and right-sided colorectal neoplasms: a casecontrol study. *J Exp Clin Cancer Res*. Jul 23 2013; 32: 44. PMID 23876008
3. Beacon Biomedical. Non-Clinical Verification and Clinical Validation of BeScreened-CRC, a Blood-Based In Vitro Diagnostic Multivariate Index Assay for the Detection of Colorectal Cancer in Screening Non-Compliant Patients. 2017.  
[https://static1.squarespace.com/static/5b8832f8f2e6b1941b7c53ac/t/5df286f293135176b05b5edb/1576175349526/BeScreened-CRC+White+Paper\\_2017\\_+201901R1.pdf](https://static1.squarespace.com/static/5b8832f8f2e6b1941b7c53ac/t/5df286f293135176b05b5edb/1576175349526/BeScreened-CRC+White+Paper_2017_+201901R1.pdf) Accessed June 20, 2021
4. U.S. Preventive Services Task Force. Colorectal cancer: screening. 2016;  
<https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/colorectal-cancer-screening>. Accessed May 27, 2021.
5. Nian J, Sun X, Ming S, et al. Diagnostic Accuracy of Methylated SEPT9 for Blood-based Colorectal Cancer Detection: A Systematic Review and Meta-Analysis. *Clin Transl Gastroenterol*. Jan 19 2017; 8(1): e216. PMID 28102859
6. Song L, Jia J, Peng X, et al. The performance of the SEPT9 gene methylation assay and a comparison with other CRC screening tests: A meta-analysis. *Sci Rep*. Jun 08 2017; 7(1): 3032. PMID 28596563
7. Hariharan R, Jenkins M. Utility of the methylated SEPT9 test for the early detection of colorectal cancer: a systematic review and meta-analysis of diagnostic test accuracy. *BMJ Open Gastroenterol*. 2020; 7(1): e000355. PMID 32128229
8. Li B, Gan A, Chen X, et al. Diagnostic Performance of DNA Hypermethylation Markers in Peripheral Blood for the Detection of Colorectal Cancer: A Meta-Analysis and Systematic Review. *PLoS One*. 2016; 11(5): e0155095. PMID 27158984
9. Yan S, Liu Z, Yu S, et al. Diagnostic Value of Methylated Septin9 for Colorectal Cancer Screening: A Meta-Analysis. *Med Sci Monit*. Sep 25 2016; 22: 3409-3418. PMID 27665580
10. Church TR, Wandell M, Lofton-Day C, et al. Prospective evaluation of methylated SEPT9 in plasma for detection of asymptomatic colorectal cancer. *Gut*. Feb 2014; 63(2): 317-25. PMID 23408352
11. Song L, Wang J, Wang H, et al. The quantitative profiling of blood mSEPT9 determines the detection performance on colorectal tumors. *Epigenomics*. Dec 2018; 10(12): 1569-1583. PMID 30426784
12. Marshall KW, Mohr S, Khettabi FE, et al. A blood-based biomarker panel for stratifying current risk for colorectal cancer. *Int J Cancer*. Mar 01 2010; 126(5): 1177-86. PMID 19795455
13. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: colorectal cancer screening. Version 2.2021.  
[https://www.nccn.org/professionals/physician\\_gls/pdf/colorectal\\_screening.pdf](https://www.nccn.org/professionals/physician_gls/pdf/colorectal_screening.pdf). Accessed May 27, 2021.
14. Wolf AMD, Fontham ETH, Church TR, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. *CA Cancer J Clin*. Jul 2018; 68(4): 250-281. PMID 29846947
15. Qaseem A, Crandall CJ, Mustafa RA, et al. Screening for Colorectal Cancer in Asymptomatic Average-Risk Adults: A Guidance Statement From the American College of Physicians. *Ann Intern Med*. Nov 05 2019; 171(9): 643-654. PMID 31683290

16. Rex DK, Boland CR, Dominitz JA, et al. Colorectal Cancer Screening: Recommendations for Physicians and Patients from the U.S. Multi-Society Task Force on Colorectal Cancer. *Am J Gastroenterol*. Jul 2017; 112(7): 1016-1030. PMID 28555630
17. Davidson KW, Barry MJ, Mangione CM, et al. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA*. May 18 2021; 325(19): 1965-1977. PMID 34003218
18. Lin JS, Perdue LA, Henrikson NB, et al. Screening for Colorectal Cancer: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA*. May 18 2021; 325(19): 1978-1997. PMID 34003220
19. National Coverage Determination (NCD) for Colorectal Cancer Screening Tests (210.3)  
<https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?ncdid=281&ncdver=6&bc=CAAAAAAAAAAAAA>

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